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EXAMINER	
KUBELIK, ANNE R	
ART UNIT	**PAPER NUMBER**
1638	14

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/743,690	Applicant(s) CHRISTELLER ET AL.	
	Examiner Anne R. Kubelik	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for R ply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-54* is/are pending in the application.

4a) Of the above claim(s) *1-15, 24-30 and 32-52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-23, 31 and 53-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *with the application* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's election of Group III (claims 16-20, 22-23, 31 and 53-54), SEQ ID NOs:6 and 7 and avidin in Paper No. 13 is acknowledged. Because Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-15, 24-30 and 32-52 are withdrawn from consideration as being drawn to non-elected inventions. Claim 21 should have been included in Group III. Because a search on Groups I and avidin also found art on streptavidin, as a courtesy to Applicant streptavidin will also be included in the examination. Claims 16-23, 31 and 53-54 are examined to the extent they read on avidin and streptavidin.

2. The title of the invention is not descriptive of the instant invention. A new title is required that is clearly indicative of the invention to which the claims are directed. Note that titles can be up to 500 characters long.

3. The abstract is not descriptive of the instant invention. A new abstract is required that is clearly indicative of the invention to which the claims are directed.

4. The drawings are objected to for the reasons indicated on the accompanying form PTO 948. Corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance. See 37 CFR 1.85(a) and MPEP 608.02(b).

Claim Objections

5. Claim16-21, 23, 31 and 53-54 are objected to because of the following informalities:

Claims 16 and 21 have an improper article before "polypeptide" in line 1.

Claims 17 and 20 start with an improper article.

Claims 18, 23 and 53 have an improper article before "DNA".

Claim 19 has an improper article before "vector".

Claim 31 has an improper article before "chimeric".

Claim 54 has an improper article before "plant".

Claim Rejections - 35 USC § 101

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claim 54 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claim is drawn to seeds, which is a product of nature.

Claim 54, as written, does not sufficiently distinguish over seeds as they exist in nature because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See *American Wood v. Fiber Disintegrating Co.*, 90 U.S. 566 (1974), *American Fruit Growers v. Brogdex Co.*, 283 U.S. 2 (1931), *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 33 U.S. 127 (1948), *Diamond v. Chakrabarty*, 206 USPQ 193 (1980). Note that half the seeds of a transformed plant will not comprise the nucleic acid with which the plant has been transformed. It is suggested that the

claims be modified to refer to the hand of the inventor, *e.g.* by stating that the seeds comprise the nucleic acid. See MPEP 2105.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 16-23, 31 and 53-54 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a multitude of nucleic acids that encode a chimeric protein comprising any vacuole targeting sequence operably linked to any "plant-noxious pest control protein", cells and plants transformed with these nucleic acids and methods of using the cells and plants to produce the protein. In contrast, the specification only describes vectors encoding the potato proteinase inhibitor I signal peptide operably linked to avidin mature peptide or potato proteinase inhibitor II signal peptide operably linked to streptavidin. Applicant does not describe other DNA molecules encompassed by the claims, and the structural features that distinguish all such nucleic acids from other nucleic acids are not provided.

The specification on pg12, lines 13-15 defines a plant-noxious protein as one that "has a negative effect on plant health, growth, development or fertility when not sequestered in a plant vacuole", but a few paragraphs latter included *Bacillus thuringiensis* toxins as such proteins. Bt

toxins are not considered to be "plant noxious" as defined above and in fact they improve plant health because they reduce attack by pests. Thus, the contradiction in the specification means it is not clear what a plant-noxious pest control protein really is, and a description of such proteins is lacking.

Hence, Applicant has not, in fact, described nucleic acids that encode a chimeric protein comprising any vacuole targeting sequence operably linked to any "plant-noxious pest control protein" within the full scope of the claims, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed compositions, it is not clear that Applicant was in possession of the genus claimed at the time this application was filed.

See *Univ. of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1997):

> The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA .... Accordingly, the specification does not provide a written description of the invention ....

and at pg 1406:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicted, does not suffice to define the genus because it is only an indication of what the genes does, not what it is.

See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at page 1021:

> A gene is a chemical compound, albeit a complex one, and ... conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials .... Conception does not occur unless one has a mental picture of the structure of the chemical or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by it principal biological property, *e.g.*, encoding

> human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

10. Claims 16-23, 31 and 53-54 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acids that encode a chimeric protein comprising any vacuole targeting sequence operably linked to avidin or streptavidin, cells and plants transformed with those nucleic acids, and methods of using the cells and plants to produce the protein, does not reasonably provide enablement for nucleic acids that encode a chimeric protein comprising any vacuole targeting sequence operably linked to any "plant noxious pest control protein", cells and plants transformed with those nucleic acids, and methods of using the cells and plants to produce the protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to nucleic acids that encode a chimeric protein comprising any vacuole targeting sequence operably linked to any "plant noxious pest control protein", cells and plants transformed with those nucleic acids, and methods of using the cells and plants to produce the protein.

The instant specification, however, only provides guidance for vectors encoding the potato proteinase inhibitor I signal peptide operably linked to avidin mature peptide (example 2) or potato proteinase inhibitor II signal peptide operably linked to streptavidin (example 3); immunodetection of avidin in transformed tobacco (examples 4-5); analysis of the toxicity of the avidin- or streptavidin-transformed tobacco plants to a variety of larvae, including potato tuber moth larvae, common cutworm, and cotton bollworm, (examples 6-9); toxicity of purified streptavidin and/or avidin proteins to pine shoot tip moth larvae, neonate clover root weevil, or

neonate argentine stem weevil (examples 10 and 13), avidin-painted leaves to neonate willow sawfly larvae or black field cricket (examples 11-12), and a demonstration that adult clover root weevils, honeybees, slugs, snails and root-knot nematodes were not harmed by a diet that contained avidin, avidin-painted leaves or transgenic (examples 14-17); and toxicity of protease inhibitor or Bt toxin-painted avidin transformed tobacco leaves to *Helicoverpa armigera* (example 18).

The instant specification fails to provide guidance for other nucleic acids that encode plant-noxious pest control proteins or plants transformed with those nucleic acids.

As discussed above, the specification on pg12, lines 13-15 defines a plant-noxious protein as one that "has a negative effect on plant health, growth, development or fertility when not sequestered in a plant vacuole", but a few paragraphs latter included *B. thuringiensis* toxins as such proteins. Bt toxins are not considered to be "plant noxious" as defined above and in fact they improve plant health because they reduce attack by pests. Thus, the contradiction in the specification means it is not clear what a plant-noxious pest control protein really is, and guidance for selection of such proteins, and nucleic acids that encode them, is lacking.

As the specification does not describe the transformation of any plant with nucleic acid that encodes a chimeric protein comprising any vacuole targeting sequence operably linked to any "plant noxious pest control protein" other than avidin or streptavidin, undue trial and error experimentation would be required to screen through the myriad of nucleic acids encompassed by the claims and plants transformed therewith, to identify those that have a negative effect on plant health, growth, development or fertility when not sequestered in a plant vacuole, if such plants are even obtainable.

Given the claim breath, unpredictability in the art, and lack of guidance in the specification as discussed above, the instant invention is not enabled throughout the full scope of the claims.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 16-23, 31 and 53-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections.

Claims 16 and 31 are indefinite for being dependent upon a non-elected claim.

Claims 16 and 21 lack antecedent basis for the limitation "polypeptide according to claim 1" as claim 1 is drawn to a chimeric polypeptide.

Claim 17 lacks antecedent basis for the limitation "said nucleic acid" in line 2.

Claims 18, 22-23 and 53 lack antecedent basis for the limitation "DNA molecule according to claim 17" as claim 17 is drawn to a nucleic acid molecule.

Claim 53 is indefinite for its recitation of "plant-noxious protein" in line 2, for the reasons indicted above

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a), which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are

such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 16-23, 31 and 53-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Raikel (1994, US Patent 5,360,726) in view of Czapla et al (WO 94/00992).

The claims are drawn to nucleic acids that encode a chimeric protein comprising any vacuole targeting sequence operably linked to avidin or streptavidin, cells and plants transformed with these nucleic acids, and methods of using the cells and plants to produce the protein.

Raikel discloses a method of targeting the pest control proteins lectin or chitinase to plant cell vacuoles using a vector encoding the vacuole targeting sequence, including that from barley lectin, and plants so transformed (column 11, line 4, to column 14, line 39; column 18, line 23, to column 26, line 4; claims 1-6). Raikel also teaches a method of isolating the protein from those cells and plants (column 19, line 55, to column 20, line 64, and column 24, line 49, to column 25, line 32). Raikel does not disclose nucleic acids that encode a chimeric protein comprising the lectin vacuole targeting sequence operably linked to avidin or streptavidin.

Czapla et al teach that plants transformed with a nucleic acid encoding avidin or streptavidin are resistant to a variety of insect larvae (pg 2, lines 10-27).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of expressing pest control proteins in the vacuole as taught by Raikel, to substitute avidin or streptavidin as the pest control protein as described in Czapla et al. One of ordinary skill in the art would have been motivated to do so because selection of pest control protein is an obvious design choice. Production of seeds from the transgenic plants is a common step in plant transformation.

15. Claims 16-23, 31 and 53-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boller et al (US Patent 6,054,637, filed June, 1991) in view of Hilder et al (1987, Nature 330:160-163), taken with the evidence of Applicant's admission.

The claims are drawn to nucleic acids that encode a chimeric protein comprising any vacuole targeting sequence operably linked to a "plant noxious pest control protein", cells and plants transformed with these nucleic acids, and methods of using the cells and plants to produce the protein..

Boller et al disclose nucleic acids encoding vacuolar signal peptides (SEQ ID NOs:1-16). Boller et al also suggest using vacuolar signal peptides to express protease inhibitors like the cowpea trypsin inhibitor, in plant vacuoles (column 17, line 50, to column 18, line 21). Boller et al teach plant transformation (column 50, line 25, to column 52, line 3), isolation of proteins form transformed cells and plants (column 52, line 5, to column 54, line 59), and seeds (column 54, lines 60-64). Boller et al do not disclose the constructs encoding the cowpea trypsin inhibitor.

Hilder et al teach constructs encoding the cowpea trypsin inhibitor and plants transformed with those constructs (pg 161-162).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of using vacuolar signal peptides to express protease inhibitors in plant vacuoles as taught by Boller et al, to express the cowpea trypsin inhibitor as described in Hilder et al in those vacuoles. One of ordinary skill in the art would have been motivated to do so because of the suggestion of Boller to do so (column 17, line 50, to column 18, line 21).

Applicant teaches that proteinase inhibitors are plant noxious pest control proteins (specification, pg 12, lines 21-35).

Conclusion

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Anne R. Kubelik, Ph.D.
November 14, 2002

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